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PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

BALDOCK, Sharon, Claire
Verulam Gardens
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London WC1X 8BT
GRANDE BRETAGNE

PCT

WRITTEN OPINION
(PCT Rule 66)

Date of mailing *(day/month/year)*	19.11.2004
Applicant's or agent's file reference SCB/61737001	**REPLY DUE within 1 month(s) and 15 days** from the above date of mailing

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/GB 03/04725	03.11.2003	04.11.2002

International Patent Classification (IPC) or both national classification and IPC
A61K31/352

Applicant
GW PHARMA LIMITED

1. This written opinion is the **first** drawn up by this International Preliminary Examining Authority.

2. This opinion contains indications relating to the following items:

I	☒	Basis of the opinion
II	☐	Priority
III	☐	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
IV	☒	Lack of unity of invention
V	☒	Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
VI	☐	Certain documents cited
VII	☐	Certain defects in the international application
VIII	☐	Certain observations on the international application

3. The applicant is hereby **invited to reply** to this opinion.

When? See the time limit indicated above. The applicant may, before the expiration of that time limit, request this Authority to grant an extension, see Rule 66.2(d).

How? By submitting a written reply, accompanied, where appropriate, by amendments, according to Rule 66.3. For the form and the language of the amendments, see Rules 66.8 and 66.9.

Also: For an additional opportunity to submit amendments, see Rule 66.4. For the examiner's obligation to consider amendments and/or arguments, see Rule 66.4 bis. For an informal communication with the examiner, see Rule 66.6.

If no reply is filed, the international preliminary examination report will be established on the basis of this opinion.

4. The final date by which the international preliminary examination report must be established according to Rule 69.2 is: 04.03.2005

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BOULT WADE TENNANT

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WRITTEN OPINION International application No. PCT/GB 03/04725

I. Basis of the opinion

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this opinion as "originally filed")*:

Description, Pages

1-8 as originally filed

Claims, Numbers

1-20 as originally filed

Drawings, Sheets

1/3-3/3 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
   ☐ the language of publication of the international application (under Rule 48.3(b)).
   ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   ☐ contained in the international application in written form.
   ☐ filed together with the international application in computer readable form.
   ☐ furnished subsequently to this Authority in written form.
   ☐ furnished subsequently to this Authority in computer readable form.
   ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
   ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☐ the description, pages:
   ☐ the claims, Nos.:
   ☐ the drawings, sheets:

5. ☐ This opinion has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

6. Additional observations, if necessary:

IV. Lack of unity of invention

1. In response to the invitation (Form PCT/IPEA/405) to restrict or pay additional fees, the applicant has:

   ☐ restricted the claims.

   ☒ paid additional fees.

   ☐ paid additional fees under protest.

   ☐ neither restricted nor paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied with for the following reasons and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees:

3. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this opinion:

   ☒ all parts.

   ☐ the parts relating to claims Nos. .

V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1, 2, 3, 4, 5 ,6, 7, 9, 11, 12, 13, 14, 15, 17, 19 No
Inventive step (IS)	Claims	1-20 (No)
Industrial applicability (IA)	Claims	1-20 (yes)

2. Citations and explanations

see separate sheet

SECTION IV
Lack of unity of invention

This IPEA agrees with the objection as to lack of unity put forward by the ISA, for the reasons already given in Form PCT/ISA/206. Since the Applicant, upon invitation, has paid an additional search fee and an additional examination fee, the present Opinion will be drawn in respect of both the two inventions identified in Form PCT/ISA/206. These two inventions relate to:
1) the use of cannabinoids in relation to the treatment of neuropathic and chronic pain
2) the use of cannabinoids in relation to the treatment of seep disturbance

INVENTION N.1

SECTION V
Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following documents; unless otherwise indicated, reference is made to the relevant passages emphasized in the Search Report.
D1 (WO02064109)
D2 (WO02069993)

NOVELTY (Art.33(3) PCT)

D1 (WO02064109, page 27, line 5-15, 27-33; page 28, line 15-17; page 28, line 34 - page 29, line 2; page 31, line 3-10; page 33, line 5-15; claims 26, 29, 45, 49, 53, 78) discloses compositions comprising cannabinoids (preferred are mixture of tetrahydrocannabinol (THC) and cannabidiol (CBD)). These compositions are used for the treatment of neuropathic and chronic pain (cancer pain). Compositions comprising a 1:1 mixture of THC and CBD are preferred for the treatment of neuropathic pain (see table 4). These compositions can be in the form of plant extracts and can be administered in the form of a sublingual or buccal spray.
In view of this prior art, the subject matter of claims 1, 2, 3, 4, 5 ,6, 9 is not new in the sense of Art.33(2) PCT.
D2 (WO02069993, page 1, line 5-10, 29-31; page 2, line 10-21; page 3, line 12-15; page 7, line 38 - page 8, line 1; page 8, line 22-33; examples 1, 2 and claims) discloses pharmaceutical compositions comprising tetrahydrocannabinol (THC) and cannabidiol (CBD) in ratio 3:1-1:2; and preferably in ratio 2:1. These compositions are used for the

treatment of chronic pain, of cancer pain and of pain occurring in multiple sclerosis. Plant extracts comprising the cannabinoids are also disclosed. Dosage forms for delivering less than 37.5 mg THC are disclosed.
In view of this prior art, the subject matter of claims 1, 2, 3, 4, 5 , 7, 9 is not new in the sense of Art.33(2) PCT.

INVENTIVE STEP (Art.33(3) PCT)

Most of the subject matter related to the first invention appears to be anticipated by D1 and D2. The subject matter which is still new (for example the selection of certain specific dosages or dosage ratios between the cannabinoids, or the treatment of certain specific forms of pain) does not seem to be characterized by any new technical feature providing surprising or unexpected technical effect over the prior art. For this reason the subject matter of claims 8, 10 does not seem to involve an inventive step in the sense of Art.33(3) PCT.
Note: since the priority of the present application appears to be valid, the intermediate document GB2377633 is not considered as prior art for establishing novelty and inventive step of the present application.

INDUSTRIAL APPLICATION

The subject matter of claims 1-10 is industrially applicable.

INVENTION N.2

SECTION V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following documents; unless otherwise indicated, reference is made to the relevant passages emphasized in the Search Report.

D2: WO 02/069993 A (WERNER MICHAE et al.) 12 September 2002
D3: WO 02/080903 A (RADULOVACKI MIODRAG et al.) 17 October 2002
D4: WO 02/056932 A (EMLIN BIOSCIENCES) 25 July 2002 (2002-07-25)
D5: DATABASE MEDLINE [Online] US NATIONAL LIBRARY OF MEDICINE (NLM), BETHESDA, MD, US; August 1981 (1981-08) CARLINI E A ET AL: 'Hypnotic and antiepileptic effects of cannabidiol.' Database accession no. NLM7028792 XP002277010 & JOURNAL OF CLINICAL PHARMACOLOGY. US 1981 AUG-SEP, vol. 21, no. 8-9 Suppl, August 1981, pages 417S-427S.

NOVELTY (Art.33(2) PCT)

D2 (WO02069993, page 1, line 5-10, 29-31; page 2, line 10-21; page 9, line 5, 6, 7; claims 1,2,3,4, 7,8,10); examples 1, 2) discloses pharmaceutical compositions comprising tetrahydrocannabinol (THC) and cannabidiol (CBD) in ratio 3:1-1:2; and preferably in ratio 2:1. The use of these compositions for the treatment of sleep disorders (insomnia) is also disclosed (see page 9, line 5,6,7). Plant extracts comprising the cannabinoids are also disclosed. Dosage forms for delivering less than 37.5 mg and less then 10 mg THC are also disclosed.
In view of this prior art, the subject matter of claims 11, 12, 13, 14, 15, 17, 19 is not new in the sense of Art.33(2) PCT.
D3 (WO 02/080903, see page 7, lines 7-19 , 25; figures 1a, 1b, 2a, 4; claims 1,5) discloses the administration of a cannabinoids (THC, 9-tetrahydrocannabinol cannabidiol being among the preferred ones), for the treatment of a sleeping disorder (a sleep related breathing disorder).
D4 (WO 02/056932, see page 4, lines 4-11, 15; claims 1, 9, 22, 23) discloses delivery devices for the administration of drugs (cannabinoids are the preferred drugs) for treatment of a number of diseases. Sleep disorders are also mentioned.
D5 (XP002277010, see abstract) discloses the hypnotic effect of cannabidiol.
In view of D3, D4, D5 the subject matter of claims 11,12 is not new.

INVENTIVE STEP (Art.33(3) PCT)

Most of the subject matter relating to the second invention claimed in the present application is anticipated by D2-D5. The subject matter which is still new (for example the selection of certain specific dosages or dosage ratios between the cannabinoids, or of certain specific forms of pain) does not seem to be characterized by any new technical feature providing any surprising or unexpected technical effect over the prior art. Also, from the data reported in the figures it appears that the administration of 1:1 ratios of THC and CBD does not provide significant differences as compared to the administration of THC alone.
For this reason the subject matter of claims 16, 18, 20 does not seem to involve an inventive step over the prior art.

INDUSTRIAL APPLICATION

The subject matter of claims 11-20 is industrially applicable.